ORODISPERSIBLE FILM: A PARADIGM SHIFT IN PATIENT CENTRIC DRUG DELIVERY

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ABSTRACT: Orodispersible Films (ODFs) or Orodispersible Strips (ODSs) are a major emerging form of new route to drug delivery (Novel Drug Delivery Systems or NDDS). Such doses are ultra-thin single or multilayer sheets of special materials. They are meant to release the drug (active pharmaceutical ingredient or API) rapidly upon contacting saliva in the mouth [1]. ODFs absorb water fast and dissolve to form a thin liquid or mixture that can be swallowed by the patient without requiring water or needing to chew [2]. This technology addresses a significant issue known as dysphagia (the inability to swallow) and assists drugs to perform their job better by enhancing the quantity of medicine the body absorbs (bioavailability). ODFs are not only important in making things easier. Through the abundant blood supply in the mouth, and due to the fact that the mouth has low concentrations of chemical action that destroys drugs, the medication can bypass the first stage of metabolism (hepatic first-pass metabolism) in the liver. This enhanced route ensures that smaller amounts of drug would be required (dose reduction) and that the drug would have a rapid action effect, and ODFs would be ideal in cases where a quick action is required such as in cases of an emergency. The technology has been applied primarily in the delivery of potent drugs that are usually in a small dose and in assisting drugs which are not readily soluble (seen as BCS Class II and Class IV in the pharmaceutical community) absorb better [4].

KEY WORDS: Orodispersible films, Mucoadhesion, Bioavailability, Amorphous Solid Dispersion, Hot Melt Extrusion.

1. INTRODUCTION:

1.1 Orodispersible films:

Orodispersible films are known for being very thin and having a specific mix of materials. They are usually sheets, either single or multilayered, and about the thickness of a postage stamp. Commercial strips are precisely made, often measuring 1 times 2 cm^2 or 2 times 2 cm^2 [2]. This small, controlled size means a lot of the film's surface area is exposed, which is essential for quickly absorbing saliva and dissolving. The recipe mainly uses water-soluble polymers, which form the film's backbone, along with other ingredients chosen to improve how the film works, its stability, and how much patients like it.

1.2 Mechanism of Dispersal and Oral Mucosal Interaction:

It is the medicine in the ODF that works, due to a special process within the mouth. The film takes up the saliva on placing it on the wet tissue, such as tongue [1]. The strip

begins to break and the drug is dissolved through this fast absorption process. Significantly, the film must have sufficient mucoadhesion (sticking ability) to adhere to the location of its application. When stuck the big surface of the strip (typically 1 to 20 cm^2) assists in absorbing the moisture immediately, fragmenting and disintegrating it promptly, dissolving and then passing through the lining of the mouth [2].The final product is a thin liquid or mixture that is subsequently consumed. The drug should work well with speed. Although first the Food and Drug Administration (FDA) recommended that similar tablets (Orally Disintegrating Tablets or ODTs) be able to disintegrate within less than 30 seconds, ODFs should also act that way. ODFs are, however, not structurally similar to hard pills. Their very slimness and high surface area provide a certain way of their own, and it may be proposed that the regulations of the future must emphasize the speed with which the product is dissolved by the resulting liquid, as opposed to the speed with which the solid strip dissolves.

Good stickiness (mucoadhesion) is important too, to the principal advantage of the drug. When ODF is not adhering properly to the mouth, it is swallowed in excessive speed. By taking the drug in a hurry, the drug is absorbed rapidly through the digestive system and processed by the liver (first-pass hepatic metabolism) first [3]. Hence, to ensure the drug enters the main system of the body without the initial processing of the liver, it is essential to stick the film well to the highly vascularized mouth to benefit better. One of the greatest shortcomings of ODFs is their capacity to carry drugs. Since the dose should be small, tasty and extremely thin, ODFs do not affect large doses as regular orally dissolving tablets (ODTs). This physical constraint implies that ODF technology should be used with potent drugs that only require a small dose or drugs that require enhancing the absorption rather than the overall drug amount.

1.3. Classification of ODFs

To manage the different medical goals this system can achieve, ODFs are sorted into three main types based on how they work and their structure:

- **Type 1 ODFs (Release Rate):** This group is sorted by how quickly the drug is released: fast, moderate, or slow. This allows the film to be customized for different needs, like needing an immediate body-wide effect versus a local or slow-release action.

- **Type 2 ODFs (Layering Architecture):** Films are grouped by their physical construction: monolayer (single layer), bilayer (two layers), or multilayer (many layers). Single-layer films are the simplest. Complex bilayer or multilayer films often include a separate layer for covering up bad taste or helping the drug absorb better, effectively sandwiching the drug layer for the best result [2].

- **Type 3 ODFs (Drug Source):** This group distinguishes films based on where the drug comes from, whether it is synthetic (man-made), such as sildenafil, or comes from natural sources, like extracts of ginger or turmeric.

1.4 Formulation Science and Excipient Architecture

Creating a commercial ODF is a challenge in material science, requiring exact control

over the film's structure to achieve two conflicting goals: making it strong enough to handle and making it dissolve quickly enough to work.

1.4.1. Film-Forming Polymers: The ODF Matrix

The core structural component, which constitutes the largest proportion of the film at up to 65% of the film dry weight, is the film-forming polymer that forms the core of a film and determines the strength of the film, the rate of dissolution, and the compatibility of a film-drug. The selection criteria is based on water solubility, forming a film, and manufacturing processes. A vast number of different water-soluble polymers are employed such as modified starches, certain types of hydroxypropyl methylcellulose (HPMC), sodium carboxymethyl cellulose (NaCMC), polyvinyl alcohol (PVA), and polyethylene oxide (PEO). These polymers should also be easily dissolved in saliva so that the drug can be liberated in time [5]. The manufacturing plan strongly depends on the polymer that is used. Softening polymers such as PEA and some types of high-molecular-weight PVAs are best used in high-speed techniques such as Hot Melt Extrusion (HME) due to their flow-ability. On the other hand, natural polymers such as pullulan usually necessitate a process known as Solvent Casting since they are unable to withstand high temperatures. Consequently, the choice of the way the film should be produced has to be made simultaneously with the choice of the polymer to make the process viable at a massive scale.

2. Theoretical Perspective and Significance of Orodispersible Films in Drug Delivery

The theory of Orodispersible Films (ODFs) has its basis on the premises of Novel Drug Delivery System (NDDS) designed to get around the shortcomings of the traditional or traditional oral dosage delivery forms like tablets and capsules. ODFs theoretical framework is developed on the basis of the principle of pharmacokinetic rapid disintegration and mucosal absorption, according to which, the maximum efficiency of drug delivery should occur, with minimum degradation and maximum bioavailability. As opposed to the usual forms of dosage, which have to be subjected to the first round of hepatic metabolism upon swallowing, ODFs cause the drug to pass directly into the systemic circulation via either the buccal, sublingual/palatal mucosa, effectively bypassing the first-pass hepatic metabolism. Such a special administration route increases the efficacy of the therapeutic effect, provides high rates of rapid action, and a reduction of dose loss, as ODFs are an essential breakthrough in patient-centered pharmaceutical design.

In the perspective of the theory of formulation, ODFs can be considered as a development in the sphere of mucosal drug delivery, which merges the ideas of polymer chemistry, surface science, and bioadhesion kinetics. The large ratio of surface-volume ratio of the film increases the rate of dissolution and this is in line with the equation of Noyes-Whitney equation where the rate of dissolution of a solute increases with the more surface of the solute, which in this case is saliva. Moreover, the intensive contact of the drug-loaded film and wet oral mucosa is guaranteed by the presence of mucoadhesive polymers, which increase the residence time and local absorption. The entrapment of saliva constituents, saliva components and mucin layers between the polymer matrices, hence, forms a controlled microenvironment which facilitates rapid dispersion and slow delivery (depending

on the preferred pharmacological activity). This is a fine balance between mechanical strength and dissolution kinetics, which is a fundamental issue and a notable strength of ODF technology.

With respect to clinical use, ODFs have proven to be very beneficial in addressing acute and chronic diseases which demand urgent therapeutic care or enhanced patient adherence. Examples can be seen in the case of Rizatriptan, Sumatriptan and Eletriptan ODFs in treating migraine, giving a faster onset compared to traditional tablets, Ondansetron ODFs in rapid management of nausea and vomiting in chemotherapy, Sildenafil ODFs in treating erectile dysfunction, which is more convenient and gives faster bioavailability, and finally Donepezil ODFs in the treatment of Alzheimer, which is easier to administer in the elderly population. In addition to this, Clozapine, Olanzapine and Aripiprazole ODFs have been established in order to increase the tendency of adherence in psychiatric treatment whereas Loratadine, Cetirizine and Montelukast ODFs are employed in the management of allergy and asthma to enable a quicker symptomatic treatment. ODFs are widely used in pediatric and geriatric patients, where swallowing challenges are prevalent, and are safer and more acceptable by patients.

In general, scientific and therapeutic contribution of the ODFs consists in the fact that they combine the material science innovation with clinical effectiveness. ODFs have revolutionized the concept of ODs in terms of rapid dissolution, greater bioavailability, and patient convenience. The design flexibility enables them to be custom designed as prompt, delayed or targeted drug delivery and is a next generation platform of accurate, efficient, and convenient medication delivery.

3. Functional Excipients and Property Modulation

To perform optimally, ODFs need a carefully chosen set of functional ingredients (excipients):

a. **Plasticizers (Flexibility Agents):** Ingredients like poloxamer 407, poloxamer 188, and polyethylene glycol are essential for making the film flexible and improving its strength. Good flexibility directly impacts the folding endurance—a key test that measures how many times a film can be folded before breaking—which is vital for the film to survive manufacturing, packaging, and handling by the patient.
b. **Superdisintegrants (Breakdown Accelerators) and Saliva-Stimulating Agents:** These chemicals speed up the main action of the strip. Saliva-stimulating agents increase the moisture available , while superdisintegrants or surfactants, like Poloxamer 188, are used to make the strip dissolve immediately.

Some ingredients often do more than one job. For example, Poloxamer 188 acts as both a flexibility agent and a breakdown accelerator and has been shown to dramatically speed up the dissolution time in some recipes. This speed increase is often linked to the excipient helping the drug stay in a highly soluble, non-crystalline form (called an amorphous solid dispersion or ASD) within the polymer matrix [4]. This shows that choosing ingredients is not just about optimizing physical strength but also a critical way to improve how well the drug works biologically.

A successful ODF product depends heavily on how its parts work together, as shown below. **Table 1: Primary Components and Functional Roles in ODF Formulation**

Component Class	**Example Materials**	**Primary Functional Role**	**Critical Quality Impact**
Film-Forming Polymers	HPMC, PVA, Pullulan, PEO	Forms the main structure; controls how fast the film dissolves	Determines how strong the film is (e.g., if it can be folded) and how fast it dissolves
Plasticizers	Polyethylene glycol (PEG), Glycerol, Poloxamers	Makes the film flexible and stretchy	Ensures the film doesn't break easily during handling, and remains stable over time
Superdisintegrants	Poloxamer 188, Sodium Starch Glycolate (SSG)	Makes the strip rapidly soak up saliva and break apart	Controls the time it takes to dissolve and how it feels in the mouth
Taste-Masking Agents	Flavorants, Specific Polymer Layers [3].	Covers up the bitter or bad taste of the drug	Makes the product pleasant to take [4].

4. Strategies for Solubility and Stability Enhancement

Patient compliance requires effective taste masking, especially when the drug tastes bitter. This can be done using specific flavors, sweeteners, or by building the strip with multiple layers that sandwich the drug.

For difficult drugs, especially those classified as BCS Class II or IV, maximizing dissolution (how fast it dissolves) is vital. ODFs are strategically designed to keep the drug in a non-crystalline, highly absorbable state within the polymer matrix, forming ASDs. This non-crystalline form significantly increases how quickly the drug dissolves when it touches saliva, thereby boosting the amount of drug ready for absorption through the oral lining.

However, the key feature that makes ODFs successful—the use of highly water-soluble polymers for quick dissolution —is also what creates its main stability problem. These polymers (like HPMC and PVA) naturally absorb moisture. This makes the finished ODF product very vulnerable to moisture-induced breakdown, meaning it needs specialized, high-barrier packaging, usually aluminum foil, to protect the drug from light, heat, moisture, and degradation. The need for specialized airtight packaging makes manufacturing more complicated and adds cost and difficulttheiry to long-term storage [2].

5. Biopharmaceutical Performance and Pharmacokinetic Advantages

ODFs are a valuable step forward in drug development because they offer crucial adjustments to how the drug works in the body (pharmacokinetic or PK profile), giving benefits beyond just patient convenience.

5.1. Enhancing Bioavailability through Oral Mucosal Absorption

Its biological characteristics such as the extensive blood capillary network and low concentration of enzymes that degrade drugs in the mouth position it as an ideal structure of drug intake. This condition aids the drug to enter at a fast rate and directly into the main blood stream.

The determining advantage of the pharmacological effect is the possibility to avoid the initial hepatic processing (hepatic first-pass metabolism). Medications taken by cheek (buccal) or under the tongue (sublingual) enter directly into the primary circulation without the initial passage through the liver which typically cleanses up much of the dose delivered in a standard pill. This decreased loss of the drug before getting to the bloodstream naturally enhances the absolute bioavailability of the drug, i.e., such small dose of the drug can produce the same effect of the therapeutic effect in the body [6].

The form of delivery is particularly adapt in drugs that belong to the BCS category of Class II (low solubility and high permeability) and Class IV (low solubility and low permeability). In the case of Class II drugs, the dissolving properties of the ODF are as rapid as possible, ensuring that the maximum concentration is available to be absorbed across the mouth lining. In the case of Class IV drugs, it is better that the drug should be absorbed to the greatest extent before the residue undergoes swallowing and exposure to the harsh digestive tract (GIT) in order to make the drug viable.

By removing a major percentage of loss in the liver, it is possible to maximize the dose. Assuming that a drug normally has its potency reduced by 80% through liver processing when it is swallowed, it might make a lot of sense to turn it into an ODF that induces 50% absorption in the mouth and thereby reduce the dose by a significant margin. The approach spares money on the drug material and may even decrease the total drug content in the body which can enhance safety and decrease side effects.

5.2. Pharmacodynamics and Clinical Impact

The rapid degradation and direct absorption of the dissolved drug by the greatly absorbent lining of

the mouth leads to a very rapid onset of action characterized by a shortening of the time that is required to achieve maximum concentration in the blood (Tmax). This property renders ODFs a perfect dose form to be used during acute or emergency cases because rapid therapeutic response is required. In addition, the ODF technology could assist in the delivery of short-life drugs in the human body, making the procedure easier to the patients who are required to administer medicine regularly.

The oral route has certain chemical restrictions, even though it is beneficial biologically. Even though the enzyme activity in the mouth is low, the pH (acid level) is almost neutral (usually, 6.27.4) [3]. Chemically labile drugs at this pH are not usually suitable to form as ODF or have to undergo elaborate stabilization measures to stabilize them until absorption. ODFs can be used not only in traditional small-molecule drugs. Recent research indicates that they can serve as a medium through which sensitive biological products can be delivered such as vaccines. Studies cited use of ODFs that contained a rotavirus vaccine, which are targeted at infants in the areas where it is hard to maintain cold and sterile injections. This application presents the versatility of the ODF platform to global public health activities.

Table 2: Comparative Biopharmaceutical Profile: ODFs vs. Conventional Oral Dosage Forms

Characteristic	ODF/ODS	Conventional Tablet (Immediate Release)	Strategic Advantage
Administration Requirement	No water, no chewing needed	Requires water and swallowing whole	Much easier to take, especially for people who struggle to swallow or in urgent situations [1].
First-Pass Metabolism	Avoids it partially or fully (through mouth lining)	Goes through extensive initial processing by the liver	More drug enters the bloodstream, so a lower dose is often possible, and the drug works better
Absorption Surface Area	Large, focused area in the mouth, immediate start	Mainly the digestive tract	Drug is released and enters the body quickly, maximizing how much can be absorbed
Dosage Flexibility	Limited to low doses	Can contain high doses	Best for powerful drugs or those that need only a small amount [2] [4].

6. Detailed Review of Solvent Casting

Solvent casting is the traditional and widely used industrial method for making ODFs. The process involves dissolving or mixing the ingredients and the drug in a suitable liquid (solvent), often water, though sometimes organic solvents are needed. The resulting mix is spread into a smooth layer, followed by a crucial drying step to evaporate the solvent and set the film structure [6].

Solvent casting offers a lot of flexibility in creating the formula and is good for drugs that can't handle heat. Films made this way often feel smoother and have a more evenly spread flexibility agent (plasticizer). However, scaling up this technique is challenging, especially in controlling how long and consistently the drying step takes. Furthermore, handling large amounts of solvents creates environmental and safety issues, and the method is often restricted when making films with drugs that don't dissolve easily unless very specialized liquids are used [8][9].

6.1. Hot Melt Extrusion (HME): A Continuous and Sustainable Platform

Another key innovation in ODF production is Hot Melt Extrusion (HME), which is a single-step process that produces no solvents, and is continuous. This is one of the methods where the drug and the ingredients are fed into a twin-screw machine (extruder) where a combination of heat and extreme mechanical mixing is

applied to melt the polymer base and blend the components. The liquid mixture is then forced out through a film, which is allowed to cool and cut [10].
HME is much desired due to the benefits:
1.Green: It also does not require solvents and therefore, it is safer and more environmental friendly.
2.Increased Quality: The high mixing rate within the extruder makes sure that the final batch has high uniformity of the content (uniform dose) throughout. This is the quality aspect of reliability and dose precision which is one of the most essential features in the eyes of regulatory entities.
3.Scalability and Cost-Effectiveness: HME can be replicated and scaled to any commercial production size with ease and means that fewer processing steps are required and costs decrease over time.
Moreover, HME is spectacularly effective in improving the drug absorption owing to the fact that it is a potent means of producing high drug solubility, non-crystalline drug dispersions (ASDs) essentially in the process. The high heating and cooling rate of extrusion is employed to keep the drug as an amorphous high solubility in the polymer structure.

7. Comparison of Manufacturing Methodologies.

The Solvent Casting or HME is a decisive strategic choice which influences the long term sustainability of the product in terms of costs, stability and quality of the product. Although Solvent Casting works well when trying out a first time, HME is a better route towards large scale commercial production since it is durable, solvent-free and has high quality.
HME assists in resolving a number of regulatory issues simultaneously. Getting rid of solvents, it does not raise the question of residual solvents. It offers improved dose consistency thereby making it conform to accurate dosing needs. This is an efficient process that is also coherent with current Quality-by-Design (QbD) principles. There is a trade-off in stability though, which is minor. Although Solvent casting is capable of creating films with superior initial feel and plasticizer spread, it can be susceptible to the drug re-forming into a less soluble crystalline form when in a high humidity condition than HME films. This implies that the HME process, though possibly producing a mildly less smooth film, could end up with a chemically stronger end product throughout its shelf life. The cumulative effect on the efficiency and cost characteristics of ODFs, which are mostly propelled by scalable operations, such as HME, and the prospects of a reduced dose of drugs, underlines the competitiveness of the technology to existing oral pills [11].

Table 3: Comparative Analysis of ODF Manufacturing Technologies

Feature	**Solvent Casting**	**Hot Melt Extrusion (HME)**	**Implication for Industry**
Solvent Requirement	Needs solvents (usually water)	No solvents needed	HME is safer for the environment and has lower post-production costs.
Scale-Up Feasibility	Difficult, complex drying step	Easy to scale up, continuous process	HME is the best method for making large commercial quantities.
Content Uniformity	Depends on how evenly the mix is dried and the solution is made	Better due to intense mixing in the machine	HME provides more accurate dosing, increasing regulatory trust.
Thermal Sensitivity	Good for drugs that are sensitive to heat	May be limited by the high heat of the machine	Whether the drug can handle heat determines the method used.
Film Structure/Texture	Smoother, more even plasticizer distribution	Works well, but may have slight differences in flow	Affects how the product feels and is handled [11].

8. Quality Assurance, Critical Quality Attributes (CQAs), and Regulatory Landscape

Keeping the product quality high requires strict control over the most important steps in the process (Critical Process Parameters or CPPs), which directly impact the most important features of the finished product (Critical Quality Attributes or CQAs) [12]. For ODFs, these CQAs focus on making sure the film is strong enough for shipping and handling, and that it dissolves quickly enough to work effectively [13].

8.1. Evaluation of Critical Physicochemical Properties

The main tests for ODF performance relate to speed and durability:

- **Disintegration Time and Dissolution:** The speed at which the film breaks down and dissolves in saliva is the most important factor. While guidelines recommend a quick breakdown (often less than 30 seconds) , the subsequent dissolution must also be fast to make the drug available for absorption in the mouth. Special lab equipment is used to measure these times accurately.
- **Mechanical Strength (Folding Endurance):** ODFs are naturally fragile because they are so thin. Folding endurance measures how many times a film can be folded back on itself without breaking, which directly shows its physical strength. This test is essential for ensuring the strip survives packaging, shipping, and being handled by the patient. A well-designed formula can achieve high folding endurance (e.g., 481 times) along with quick breakdown (e.g., 42.6 seconds).
- **Content Uniformity (Consistent Dose):** Ensuring that every strip contains the same, correct dose of the drug is vital, especially for low-dose, high-potency medicines. Manufacturing methods like HME, which offer intense mixing, are preferred for achieving excellent dose consistency.

A major challenge in making ODFs is the conflict between strength and speed. A film made to be very strong (high folding endurance), often by using more polymer or plasticizer, might become too stiff, which stops it from quickly dissolving. Conversely, making a strip dissolve extremely fast can make it too brittle to handle easily. Therefore, the best development requires finding a perfect balance that ensures high folding endurance (durability) and quick disintegration (performance) [14].

8.2. Stability and Packaging Requirements

The fact that the necessary film-forming polymers (like HPMC, PVA, and PEO) naturally absorb moisture makes sensitivity to moisture the biggest problem for long-term storage. Moisture getting into the package can lead to the drug breaking down, the film dissolving early, or the drug returning to its non-soluble crystalline state.

Consequently, ODFs require very specialized, protective packaging. Aluminum foil is the most common and ideal primary packaging because it provides a strong barrier against light, heat, and moisture. Achieving long-term storage is complicated and requires storing the packaged films in secondary containers to keep them completely airtight.

Given this extreme moisture sensitivity, the packaging process itself becomes a Critical Process Parameter (CPP). Any mistake in controlling the humidity during the packaging line operation or any failure in the final seal integrity can ruin the entire batch. Therefore, strong quality control rules must not only cover the chemical formula but also the strict control over the packaging environment and material integrity.

8.3.Regulatory Framework for Orodispersible Dosage Forms

Regulatory bodies worldwide recognize ODFs as a specialized dose form. The World Health Organization (WHO) and European Medicines Agency (EMA) define these forms as ones placed on the

tongue where they quickly break down into small pieces or dissolve in saliva to be swallowed. FDA guidance focuses generally on Orally Disintegrating Tablets (ODTs), setting the expectation for convenience, rapid breakdown, and helping patients with swallowing difficulties. For all immediate-release pills designed to enter the bloodstream, *Bioequivalence* (BE), meaning the drug works the same way as the original drug, must be proven. ODFs are subject to strict BE assessments aligned with international rules, such as the ICH M13A Guideline. This usually requires specific studies to prove they are therapeutically equal to the original product [14].

Strategically, ODFs give manufacturers a way to extend their legal protection (intellectual property). By remaking an established drug, like sildenafil, into a preferred ODF, often using advanced techniques like HME or new polymer mixes, companies can get new patents for the specific formula, the manufacturing method, and the resulting better drug performance. This approach is a powerful tool for managing a product's life cycle and staying competitive in the market [15].

Table 4: Critical Quality Attributes (CQAs) and Performance Metrics for ODFs

Critical Quality Attribute	Required Test	Standard/Target Metric	Primary Rationale
Disintegration Time	Test in the lab (or simulated saliva test)	Must break down quickly (Recommended: less than 30 seconds)	Ensures the drug starts working fast and meets regulatory standards.
Mechanical Strength	Folding Endurance Test	Must tolerate being folded many times (e.g., more than 100 folds)	Prevents the film from breaking during packaging, shipping, and when the patient uses it.
Content Uniformity	Chemical test (HPLC Assay) of many strips	Very little difference in dose between strips (e.g., USP requirements)	Guarantees accurate dosing, which is crucial for low-dose, powerful drugs.
Moisture Content/Stability	Tests for water content and long-term storage	Keep water content low/maintain the drug's original form	Essential for protecting the film from moisture and preventing the drug from becoming less soluble.

9. Strategic Adoption, Market Applications, and Future Innovations

9.1.Therapeutic Applications and Commercial Landscape

The market position of ODFs is driven by meeting patient needs.The ability to take medication without water or chewing greatly improves compliance, especially for people who have trouble swallowing, such as the elderly and children.

The improved drug action, which results in a quick start of effect, makes ODFs invaluable in urgent care settings. This technology is currently used in various medical areas. Examples include drugs for the central nervous system (CNS) like sildenafil citrate and tadalafil, vitamins and supplements (methylcobalamin, vitamin D3), and anti-diabetic drugs like teneligliptin hydrobromide hydrate. Further work is focused on creating ODFs for major public health treatments, including combination therapy strips for HIV/AIDS and tuberculosis [17].

Using ODF technology is a key strategy for managing the life cycle of existing drugs. By successfully remaking an established drug, such as sildenafil, into an ODF that patients prefer, companies can set their product apart, secure new patents based on the new delivery method, and stay competitive long after the original drug patent expires [18].

9.2. Pharmaceutical apllications

Orodispersible Films (ODFs) have diverse and expanding applications in pharmaceuticals, primarily for rapid, convenient, and patient-friendly drug delivery.

1) **Patient-Centric Drug Delivery:** ODFs are designed to dissolve quickly in the mouth without water, making them ideal for populations with swallowing difficulties, such as children, the elderly, and patients with dysphagia or neurological disorders. This enhances compliance and convenience compared to traditional tablets or capsules.

2) **Local and Systemic Drug Delivery:** ODFs can deliver drugs for both local (oral cavity) and systemic (through mucosal absorption) effects. They are used for rapid onset of action in conditions like migraines, asthma attacks, angina, and intraoral diseases, as well as for chronic therapies.

3) **Broad Range of Therapeutic Areas**

ODFs have been formulated for:

- Analgesics, antiemetics, antihistamines, antihypertensives, sedatives, and antipsychotics
- Treatments for schizophrenia, Parkinson's, Alzheimer's, allergies, tuberculosis, erectile dysfunction and more.
- Delivery of probiotics, vaccines, herbal extracts, and nutritional supplements[30].

4) **Personalized and Pediatric Medicine:** ODFs support individualized dosing and are suitable for personalized medicine, including compounding pharmacies and small-batch preparations. They are especially valuable for pediatric and geriatric patients, and those with dietary restrictions or allergies.

5) **Technological Innovations**, Recent advances include:

- 3D printing and multilayer films for combining incompatible drugs.
- Incorporation of nanoparticles for enhanced drug delivery.
- Prolonged and controlled release formulations.
- "Tandem films" for multi-compartment dosing[29].

6) **Commercial and Regulatory Aspects:** ODFs are available as both prescription and over-the-counter products globally, with a growing market and ongoing innovation in formulation and manufacturing.

9.3. Challenges in Dose Loading and Stability Management

Despite their benefits, ODFs face several major hurdles that prevent them from being used for all drugs:

- **Dose Limitation:** The need to keep the strip thin and small limits the total amount of drug that can be put in it, restricting ODF use to powerful or low-dose compounds.

- **Environmental Stability and Cost:** The moisture-absorbing nature of the polymer matrix requires expensive, specialized packaging (aluminum foil) and strict environmental control throughout the supply chain, complicating long-term storage and increasing material cost.

- **Formulation Complexity:** Balancing the many essential requirements—quick breakdown, high strength, drug stability at the mouth's pH, and affordability—requires a very careful and complex development process [19].

9.4. Convergence with Advanced Technologies

To give ODFs the competitive advantage in the future, the definition of these tools as a mere compliance tool should be altered to a highly accurate delivery platform, which is possible through its integration with sophisticated technologies.

- **Nanomedicine Integration**

One of the methods by which the issue of dose limitation can be solved is nanotechnology, especially when it involves the usage of small carriers such as Lipid Nanoparticles (LNPs) . A larger dose of drug can be packed inside such nanocarriers allowing to achieve a higher drug payload to the ODF strip without affecting the physical properties and rapid dissolution behavior of the strip [22]. In addition to adding load, nanoparticles can be formed to enable a specific cell or tissue to be located, engineered to bind to a predetermined target of the cell or tissue and therefore reducing side effects and making the treatment more efficient [21].

- **Personalized Medicine (PM)**

ODFs combined with nanocarriers ensure that the platform falls right in the novel area of personalized medicine (PM). PM will focus on individualizing therapy, delivering the right drug at the right dose to the right patient according to his/her genetic composition and molecular picture. Nanomedicines that are administered through ODFs can be tailored according to certain patient information, using the accuracy of the delivery platform [7].

- **AI-Driven Formulation**

Artificial intelligence (AI) is rapidly emerging as an important resource in the optimization of the development of ODF. The programs based on machine learning can accelerate the formulation process by estimating the most suitable combination of polymers and nanocarriers to provide the desired quality properties of particular drugs or patients [27]. AI is also used to discover patient-specific markers enabling nanocarriers to be tailored to ultra-precise treatment results.

ODFs combined with nanocarriers and computer optimization is a strategic change. Competitive strength of ODFs will become more and more due to their capability to provide complex and personal nanomedicines, which are not limited to simple solutions to swallowing and are situated in the high-value and precision treatment domain [28]. Additionally, the natural defense provided by the addition of nanocarriers may be a crucial logistical advantage. Assuming that nanocarriers have the ability to protect the sensitive pharmaceuticals in the film, it can potentially address the severity of moisture sensitivity of the traditional ODFs and distribution can be simplified, and the technology can be more resistant to harsh conditions in which complex packaging and humidity control are not feasible, as in the case of global vaccine delivery programs.

10. Case studies

I. Case Studies Showing Pharmacokinetic Improvement with Orodispersible Film

Sr.No.	Drug	Problem in Conventional Form	ODF Strategy	Outcome	References

1.	Risperidone	Poor solubility, compliance issues	Solid dispersion in HPMC	Faster dissolution, improved bioavailability	29
2.	Ondansetron	First pass metabolism	Buccal absorption via ODF	Rapid onset, higher bioavailability	30, 31
3.	Aripiprazole	Low solubility	Nanoparticle-loaded ODF	Enhanced solubility and faster release	32, 33
4.	Sildenafil	Variable absorption	ODF with cyclodextrin inclusion	Improved dissolution and bioavailability	34,35
5.	Ibuprofen	Poor water solubility	ODF with surfactants	Faster drug release, better patient compliance	36
6.	Zolmitriptan	Migraine therapy, needs fast onset	Thin polymeric ODF	Rapid absorption, bypasses GI metabolism	37,38

II. Case Studies Showing different formulation strategies

Sr.No.	Case study	Drug Focus	Formulation Strategy	Outcome	References
1.	3D-Printed Silica ODFs	Poorly Soluble Drugs	Porous silica matrices via 3D printing	Enhanced dissolution & drug release	40,41, 42
2.	HPMC-Based ODFs	General drugs	Solvent casting with HPMC + excipients	Rapid disintegration, better solubility	43, 44, 45,46,60
3.	ARV-110 ODFs	Anticancer PROTAC	ODF delivery system	Improved bioavailability & mucosal absorption	47

III. Case Studies showing Solubility Improvement using different Excipients with Orodispersible Film

Sr.No.	Drugs	Excipients used	Mechanism of solubility improvement	Key Findings	References
1.	Granisetron (antiemetic)	Hydroxypropyl methylcellulose (HPMC), Polyethylene glycol (PEG 400), Super disintegrants (Crospovidone)	PEG acts as a plasticizer and solubilizer; crospovidone accelerates disintegration	Rapid disintegration and improved bioavailability compared to conventional tablets	48
2.	Dexamethasone (poorly soluble corticosteroid)	3D-printed silica-based porous matrices	Silica creates macroporosity, enhancing wettability and dissolution	Significant increase in dissolution rate of dexamethasone in ODF compared to non-porous films	39
3.	Metoclopramide (antiemetic)	Pullulan, Mannitol, Sodium starch glycolate	Mannitol improves palatability and solubility; pullulan provides fast disintegration	Faster onset of action and improvedpatient compliance	49
4.	Domperidone (antiemetic)	Maltodextrin, Polyvinylpyrrolidone (PVP K30), Citric acid	PVP acts as solubilizer via solid dispersion; citric acid enhances dissolution by pH modulation	Enhanced solubility and faster drug release compared to plain drug films	49
5.	Dexamethasone (alternative study)	Eudragit polymers, Cyclodextrins	Cyclodextrins form inclusion complexes improving solubility; Eudragit controls release	Improved dissolution profile and better drug stability	50

IV. Case Studies showing Pharmacodynamics Improvement with Orodispersible Film

Sr.No.	Drugs	Excipients	Pharmacodynamic improvement	References
1.	Dimethyl Fumarate (MS)	Chitosan -alginate nanoparticles	0.6-fold higher bioavailability	51
2.	Loratadine (Antihistamine)	Nanoparticulate formulation in ODF	1.8-fold higher Cmax, 5.8-fold higher AUC, 5.1-fold longer half life	52
3.	Nebivolol (Antihypertensive)	Sodium alginate, xanthan gum, guar gum	Faster disintegration, higher AUC and Cmax vs. tablets	53
4.	Tadalafil (BPH)	Niosomal (non-ionic surfactant) film	18% higher bioavailability, faster Tmax	54
5.	Ebastine (antihistamine)	Poloxamer-188/TGPS-1000 mixed micelles	2.18-fold higher bioavailability	55
6.	Repaglinide (antidiabetic)	Hexyl alginate derivative	1.8-fold higher AUC, 2-fold higher Cmax, Faster Tmax	56
7.	Febuxostat (Antigout)	Self-nanoemulsifying system, PVP K30	2.4-fold higher bioavailability	57
8.	Ledipasvir/sofosbuvir (antiviral)	HPMC E15 solid dispersion in ODF	Higher dissolution and AUC than tablets	58
9.	Meloxicam (analgesic)	HPMC, Sodium alginate, disintegrants	Polymer type affected release	59

11. Conclusion

Orodispersible Films have proven to be a mature and strategically important Novel Drug Delivery System, fundamentally changing how drugs are taken orally by focusing on patient ease and improving drug absorption.

1. **Patient Ease and Drug Absorption:** The main strength of ODFs is their dual benefit: making it much easier for patients to take their medicine by removing the need for water or chewing, and making more drug available to the body by using mouth absorption to bypass the liver's initial processing. This makes ODFs the preferred delivery system for children, the elderly, and in acute situations, especially for drugs that don't dissolve easily (BCS Class II and Class IV compounds).

2. **Manufacturing Shift:** The pharmaceutical industry clearly favors Hot Melt Extrusion (HME) over the

traditional Solvent Casting for commercial ODF production. HME provides more consistent dosing, is environmentally friendly, and is easily scalable, directly leading to better cost efficiency and stronger quality control.

3. **Key Limitations:** The main technological problems are the strict limit on how much drug can be loaded due to the film's size , and the extreme moisture-absorbing nature of the polymer base, which requires expensive, specialized packaging (like aluminum foil) and strict process control for long-term stability.

4. **Future Direction:** The future path for ODF technology is toward complex precision medicine. The strategic combination of nanotechnology, using nanocarriers to increase drug load and enable targeted delivery, along with AI-driven formula optimization, promises to turn ODFs into platforms capable of delivering highly customized and effective treatments based on individual patient needs.

12. REFERENCES:

1. Öza.kar RS, Öza.kar E. Curr.ent overview of oral thin fil.ms. Turk.ish jour.nal of pharmac.eutical scie.nces. 2021 Feb 25;18(1):111.
2. Jac.ob S, Bod.du SH, Bhan.dare R, Ahm.ad SS, Nair AB. Orodisp.ersible fil.ms: curr.ent innovations and emer.ging tre.nds. Pharmac.eutics. 2023 Dec 11;15.(12):2753.
3. kum.ar Vishwa.karma P, Desh.kar P, Lal N, Dhudkewar S. Ora.lly Disinte.grating Str.ips (ODS) Conven.ience of Liq.uid Dos.age Form and Dose Accu.racy of Sol.id Dos.age Form.
4. Fer.lak J, Guze.nda W, Osma.łek T. Orodisp.ersible films—.Current sta.te of the art, limita.tions, adva.nces and fut.ure perspe.ctives. Pharmac.eutics. 2023 Jan 20;1.5(2):361.
5. Sal.awi A. An insi.ght into prepar.atory meth.ods and characte.rization of orodisp.ersible fil.m—A rev.iew. Pharmace.uticals. 2022 Jul 9;15.(7):844.
6. Yuan C, Sha H, Cui B. Ora.lly disinte.grating film: A new appr.oach to nutrit.ional suppleme.ntation. Food and Biopr.ocess Technology. 2022 Dec;15(.12):2629-45.
7. Algh.amdi MA, Fall.ica AN, Virzì N, Kesha.rwani P, Pitt.alà V, Gre.ish K. The prom.ise of nanotec.hnology in person.alized medi.cine. Jour.nal of person.alized medi.cine. 2022 Apr 22;1.2(5):673
8. TV F, Selva.raju K, Gowris.ankar NL. Meth.ods of Prepar.ation and Characte.rization of Orodisp.ersible Film: A Rev.iew. Syste.matic Reviews in Phar.macy. 2023 Apr 1;14(5).
9. Budh.raja U, Ang.ane P, Sha.ikh MF, Mishra A. Microencapsulation Techn.ology in Food, Pha.rma and Cosme.tics. Asi.an Jour.nal of Phar.macy and Techn.ology. 2025 Apr 26;15(2):166-72.
10. Nagendra R, Shee.tal P, Nand.itha VV, Venka.tesh K. Oral Disinte.grating Film: A Rev.iew.
11. Reut.her M, Rol.let N, Debea.ufort F, Cham.bin O. Orodisp.ersible fil.ms prep.ared by hot-.melt extru.sion ver.sus solv.ent cast.ing. International Jour.nal of Pharmac.eutics. 2025 Apr 30;675.:125536.
12. Nam JH, Kim BH, Shaf.ioul AS, Jin M, Cho CW. A comprehensive rev.iew of oral disinte.grating film prod.ucts, and the.ir qual.ity asses.sment and develo.pment. Jour.nal of Pharmac.eutical Investi.gation. 2025 May;55(3):351-73.
13. Wasil.ewska K, Winn.icka K. How to ass.ess orodisp.ersible film qual.ity? A rev.iew of appl.ied meth.ods and the.ir modific.ations. Acta Pharmac.eutica. 2019 Jun 30;69.(2):155-76
14. Bich.ave A, Pha.te S, Naik V, Gaik.wad A, Choudhary L, Choud.hary U, Pat.il S. Evalu.ation Param.eters For Mou.th Disso.lving Fil.ms
15. https://www.ema.europa.eu/en/documents/scientific-guideline/ich-m13a-guideline-bioequivalence-immediaterelease-solid-oral-dosage-forms-step-5_en.pdf
16. M13A Bioequi.valence for Immediat.e-Release Sol.id Oral Dos.age For.ms | FDA
17. De Toni L, De Roc.co Pon.ce M, Frances.chinis E, Dall'.Acqua S, Padr.ini R, Real.don N, Garo.lla

A, Fore.sta C. Subli.ngual adminis.tration of silde.nafil oro-dis.persible film: new prof.iles of drug tolera.bility and pharmaco.kinetics for PDE5 inhib.itors. Front.iers in Pharma.cology. 2018 Feb 6;9:59.

18. Jac.ob S, Bod.du SH, Bhan.dare R, Ahm.ad SS, Nair AB. Orodisp.ersible fil.ms: curr.ent innova.tions and emer.ging tre.nds. Pharmac.eutics. 2023 Dec 11;15.(12):2753.

19. Pat.el P, Praja.pati BG, Pat.el D. Mou.th disso.lving film as a poten.tial dos.age form for paedi.atric usa.ge. Jour.nal of Pharmac.eutical and Biolo.gical Scie.nces. 2023;11(2):133-41.

20. Pat.el K, Bar.ot S. Adva.nces in Taste-.Masking Strat.egies for Pedia.tric Brain-.Related Dise.ase Treat.ments: Foc.us on Polym.eric Coatings in Ora.lly Disinte.grating Tablets. Interna.tional Jour.nal of Scien.tific Rese.arch and Techn.ology. 2025 Jan 28.

21. Gangav.arapu A, Tapia.-Lopez LV, Sar.kar B, Pena-Zacarias J, Badru.ddoza AZ, Nurun.nabi M. Lip.id nanopar.ticles for enhan.cing oral bioavail.ability. Nanos.cale. 2024;16(.39):18319-38.

22. Babu BR, Pran.itha M. Formul.ation and Evalu.ation of Sol.id Lip.id Nanopar.ticles Loa.ded with Orli.stat for Enha.nced Oral Bioavail.ability. Math.ews Jour.nal of Pharmac.eutical Scie.nce. 2025 Jan 28;.9(1):1-4.

23. Suri K, Pfei.fer L, Cvet D, Li A, McC.oy M, Singh A, Ami.ji MM. Oral deli.very of stabi.lized lip.id nanopar.ticles for nucl.eic acid therap.eutics. Drug Deli.very and Translational Rese.arch. 2025 May;15.(5):1755-69.

24. Jahan.doost A, Das.hti R, Housh.mand M, Hoss.eini SA. Utili.zing mach.ine lear.ning and molec.ular dyna.mics for enha.nced drug delivery in nanoparticle syst.ems. Scien.tific Repo.rts. 2024 Nov 4;14(.1):26677.

25. Pri.ya A, Kum.ar M, Narg.und SL, Muru.gan V, Gote SA, Mur.thy R, Bhar.gavi VM, Narg.und R, Narg.und SL, Malv.iya N, Buk.ka R. Nanotechnology-Enabled Thienopyrimidines: A Fron.tier in Targ.eted Drug Deli.very.

26. Dut.ta S, Kar MR, Sik.der R. Mach.ine Lear.ning Applic.ations in Nanoparticle-Based Drug Deli.very Syst.ems for Teleme.dicine Advanc.ements. Nanote.chnol Perc.ept. 202.5:21.

27. Gres.sler S, Hipfi.nger C, Part F, Pavl.icek A, Zaf.iu C, Gie.se B. A syste.matic rev.iew of nanoca.rriers used in medi.cine and beyond—d.efinition and categor.ization frame.work. Jour.nal of Nanobiotechnology. 2025 Feb 7;2.3(1):90.

28. Upad.hyay, A. et al. (2023) – Scree.ning Optimi.zation and Characte.rization of Poly.mers for Ora.lly Disso.lving Fil.ms: A Review.

29. Polonini H, Ferreira A, Raposo N, Da Silva P, Brandão M. Compatibility assessment of novel orodispersible film vehicle for personalized medicine with selected active pharmaceutical ingredients. J Pers Med. 2023;13(11):1565. doi:10.3390/jpm13111565.

30. Salawi A. An insight into preparatory methods and characterization of orodispersible film—a review. Pharmaceuticals. 2022;15(7):844. doi:10.3390/ph15070844.

31. Chen F, Liu H, Wang B, Yang Z, Chen Y, Yang L, Wang B, Jiao Z, Lin HS, Quan Y, Wang H, Xiang X. Evaluation of the impacts of formulation parameters on the pharmacokinetics and bioequivalence of risperidone orodispersible film: a physiologically based pharmacokinetic modeling approach. AAPS PharmSciTech. 2020;21(7):245. doi:10.1208/s12249-020-01728-7. PMID:32856178.

32. Hegde HV, Yaliwal VG, Annigeri RV, Sunilkumar K, Rameshkumar R, Rao PR. Efficacy of orally disintegrating film of ondansetron versus intravenous ondansetron in prophylaxis of postoperative nausea and vomiting in patients undergoing elective gynaecological laparoscopic procedures: a prospective randomised, double-blind placebo-controlled study. Indian J Anaesth. 2014;58(4):423-9. doi:10.4103/0019-5049.138977. PMID:25197110; PMCID:PMC4155287.

33. Ravi SK, Chandrakala V. Formulation and evaluation of mouth dissolving film of ondansetron hydrochloride by using superdisintegrant. Int J Pharm Res Appl. 2020;6(6):472-85. doi:10.35629/7781-0606472485.

34. Lee JH, Park C, Song IO, Lee BJ, Kang CY, Park JB. Investigation of patient-centric 3D-printed orodispersible films containing amorphous aripiprazole. Pharmaceuticals (Basel). 2022;15(7):895. doi:10.3390/ph15070895. PMID:35890191; PMCID:PMC9319750.

35. Łyszczarz E, Hofmanová J, Szafraniec-Szczęsny J, Jachowicz R. Orodispersible films containing ball milled aripiprazole-poloxamer®407 solid dispersions. Int J Pharm. 2020;575:118955. doi:10.1016/j.ijpharm.2019.118955.

36. Sansone A, Frangione V, Lanzarotti A, Cocci A, Ceruti C, Sio M, Imbimbo C, Mirone V, Schips L, Terrone C, Jannini E. Effect of the new 75-mg orodispersible film of sildenafil on erection and sexual quality of

life: insights from an observational study. Sex Med. 2023;11(1):qfac007. doi:10.1093/sexmed/qfac007.
37. De Toni L, De Rocco Ponce M, Franceschinis E, Dall'Acqua S, Padrini R. Sublingual administration of sildenafil oro-dispersible film: new profiles of drug tolerability and pharmacokinetics for PDE5 inhibitors. Front Pharmacol. 2018;9:59. doi:10.3389/fphar.2018.00059.
38. Kiran D, Gupta RA, Bargode R. Preparation and evaluation of orodispersible film containing nonsteroidal anti-inflammatory drug. World J Pharm Pharm Sci. 2024;13(1):1615-24.
39. Poluri K, Sravanthi G, Mounika M, Rafi S, Nirosha K. Formulation development and evaluation of zolmitriptan oral soluble films using 2 factorial designs. Int J Pharm Investig. 2016;6(4):201-6. doi:10.4103/2230-973X.195927.
40. Prajapati VD, Chaudhari AM, Gandhi AK, Maheriya P. Pullulan based oral thin film formulation of zolmitriptan: development and optimization using factorial design. Int J Biol Macromol. 2018;107(Pt B):2075-85. doi:10.1016/j.ijbiomac.2017.10.082. PMID:29074082.
41. Blaháčková D, Elbl J, Lammerding LC, Mašková E, Muselík J, Kašlík J, Gajdziok J. Drug dissolution enhancement using 3D-printed silica-based oral films. AAPS J. 2025;28(1):30. doi:10.1208/s12248-025-01185-9. PMID:41361598.
42. Chow K, Yuan, Chua N, Kwan, Foo WC, Häusler O, Amoussou S. 3D printing of orodispersible film for poorly soluble drugs. 2022 Mar 30.
43. Avhale GS, Thakare BN, Sheikh AA, Biyani KR. Development and evaluation of oral dispersible film. Indo Am J Pharm Sci. 2024;11(12):15395898. doi:10.5281/zenodo.15395898.
44. Tian Y, Lin J, Jing H, Wang Q, Wu Z, Duan Y. Recent progress in orodispersible films-mediated therapeutic applications: a review. MedComm Biomater Appl. 2023;4(1):e303. doi:10.1002/mco2.303.
45. Carvalho AFF, Caldeira VF, Oliveira AP. Design and development of orally disintegrating films: a platform based on hydroxypropyl methylcellulose and guar gum. Carbohydrate Polymers. 2023;299:120155. doi:10.1016/j.carbpol.2022.120155.
46. Kittipongpatana OS, Trisopon K, Wattanaarsakit P, Kittipongpatana N. Fabrication and characterization of orodispersible composite film from hydroxypropylmethyl cellulose-crosslinked carboxymethyl rice starch. Membranes (Basel). 2022;12(6):594. doi:10.3390/membranes12060594. PMID:35736301; PMCID:PMC9227285.
47. Takeuchi Y, Hayakawa F, Takeuchi H. Formulation design of orally disintegrating film using two cellulose derivatives as a blend polymer. Pharmaceutics. 2025;17(1):84. doi:10.3390/pharmaceutics17010084.
48. Colucci LA, Rodrigues L. Development of orally disintegrating films HPMC-based containing captopril: mechanical, optical and physicochemical studies. Braz Arch Biol Technol. 2022;65(5):e220073. doi:10.1590/1678-4324-2022220073.
49. Meloni V, Halstenberg L, Mareczek L, Lu J, Liang B, Gottschalk N, Mueller LK. Exploring orodispersible films containing the proteolysis targeting chimera ARV-110 in hot melt extrusion and solvent casting using polyvinyl alcohol. Pharmaceutics. 2024;16(12):1499. doi:10.3390/pharmaceutics16121499.
50. Kakad AS, Bhajipale NS, Kunjwani HK. Formulation and evaluation of orodispersible film. Int J Res Trends Innov. 2025;10(5):IJRTI2505286. ISSN:2456-3315.
51. Chitra Naik, Shraddha Sakharkar, Shital Bhosale, Dr. Ashwini Jadhav, Dr. Tushar Shelke, The Overall Review on Formulation, Evaluation and Different Types of Manufacturing of Oral Disintegrating Films, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 8, 412-425.https://doi.org/10.5281/zenodo.16738009.
52. Jacob S, Boddu SHS, Bhandare R, Ahmad SS, Nair AB. Orodispersible films: current innovations and emerging trends. Drug Dev Ind Pharm. 2021;47(9):1365-75. doi:10.1080/03639045.2021.1938894.
53. Sinha S, Garg V, S , Singh R, Dutt R. Chitosan-alginate core-shell-corona shaped nanoparticles of dimethyl fumarate in orodispersible film to improve bioavailability in treatment of multiple sclerosis: Preparation, characterization and biodistribution in rats. J Drug Deliv Sci Technol. 2021;64:102645. doi:10.1016/j.jddst.2021.102645.
54. Van Nguyen K, Dang T, Vu L, Ha N, Truong H, Tran T. Orodispersible film incorporating nanoparticulate loratadine for an enhanced oral bioavailability. J Pharm Investig. 2023;53:417-26. doi:10.1007/s40005-023-00613-2.
55. Vijayanand P, Patil B, Reddy B. Formulation and comparative pharmacokinetic evaluation of orodispersible tablets and films of nebivolol hydrochloride. J Pharm Investig. 2015;45:237-47. doi:10.1007/s40005-014-0169-5.
56. Abla K, Mneimneh A, Allam A, Mehanna M. Application of Box-Behnken Design in the Preparation, Optimization, and In-Vivo Pharmacokinetic Evaluation of Oral Tadalafil-Loaded Niosomal Film. Pharmaceutics. 2023;15(1):173. doi:10.3390/pharmaceutics15010173.

57. Islam N, Irfan M, Khan S, Syed H, Iqbal M, Khan I, Mahdy A, Raafat M, Hossain M, Inam S, Munir R, Ishtiaq M. Poloxamer-188 and d-α-Tocopheryl Polyethylene Glycol Succinate (TPGS-1000) Mixed Micelles Integrated Orodispersible Sublingual Films to Improve Oral Bioavailability of Ebastine; In Vitro and In Vivo Characterization. Pharmaceutics. 2021;13(1):54. doi:10.3390/pharmaceutics13010054.

58. Khames A. Hexyl alginate derivative, an amphiphilic innovative buccal film-forming material of promising mechanical and release characteristics for the improvement of repaglinide bioavailability. Drug Des Devel Ther. 2019;13:925-40. doi:10.2147/DDDT.S196425.

59. Habib B, El-Samiae A, El-Houssieny B, Tag R. Formulation, characterization, optimization, and in-vivo performance of febuxostat self-nano-emulsifying system loaded sublingual films. Drug Deliv. 2021;28(1):1321-33. doi:10.1080/10717544.2021.1927247.

60. Thummala U, Maddi E, Avula P. Amorphous solid dispersion of ledipasvir and sofosbuvir for enhancement of oral bioavailability. J Res Pharm. 2023. doi:10.29228/jrp.461.

61. Jadach B, Misek M, Ferlak J. Comparison of Hydroxypropyl Methylcellulose and Alginate Gel Films with Meloxicam as Fast Orodispersible Drug Delivery. Gels. 2023;9(9):687. doi:10.3390/gels9090687.

62. El-Setouhy DA, El-Malak NSA. Formulation of a Novel Tianeptine Sodium Orodispersible Film. AAPS PharmSciTech. 2010;11(3):1018-25. doi:10.1208/s12249-010-9464-2.